

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method of [^{11}C]-radiolabelling a phenothiazine compound or a phenothiazine-like compound, wherein:

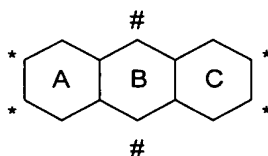
said compound has a polycyclic core of three six-membered rings fused together in a linear fashion and denoted the A-ring, B-ring, and C-ring, where the B-ring is the "middle" ring;

said polycyclic core is partially-aromatic or fully-aromatic;

said polycyclic core has 14 ring atoms, including exactly 1 or exactly 2 ring heteroatom(s), each of which is independently selected from N, O, and S;

the remainder of said ring atoms being C;

said exactly 1 or exactly 2 ring heteroatom(s) form part of the B-ring, but not part of the A-ring or C-ring, and so are located at one or both of the "central" positions denoted by a hash-mark (#) in the following depiction of the polycyclic core:



said compound has a pendant group covalently attached to a ring atom of said polycyclic core;

said pendant group is independently:

a primary amino group;

a cationic primary imino group;

a secondary amino group;

a cationic secondary imino group;

a primary imino group; or

a secondary imino group;

said method comprising the step of:

reacting said phenothiazine compound or a phenothiazine-like compound with [^{11}C]methyl trifluoromethanesulfonate ($\text{CF}_3\text{SO}_2\text{O}^{11}\text{CH}_3$);

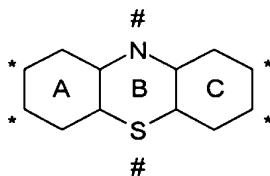
thereby converting said pendant group to a corresponding [^{11}C]methyl-labelled pendant group, respectively:

- a [^{11}C]methyl-labelled secondary amino group;
 - a [^{11}C]methyl-labelled cationic secondary imino group;
 - a [^{11}C]methyl-labelled tertiary amino group;
 - a [^{11}C]methyl-labelled cationic tertiary imino group;
 - a [^{11}C]methyl-labelled secondary imino group; or
 - a [^{11}C]methyl-labelled cationic tertiary imino group;
- to give a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.

2-62 (Canceled)

63. (New) A method according to claim 1, wherein said polycyclic core has 14 ring atoms, including exactly 2 ring heteroatoms, each of which is independently selected from N, O, and S.

64. (New) A method according to claim 1, wherein said polycyclic core has 14 ring atoms, including exactly 2 ring heteroatoms: N and S:



65. (New) A method according to claim 1, wherein said polycyclic core is fully-aromatic.

66. (New) A method according to claim 1, wherein said pendant group is independently attached to a ring carbon atom of said polycyclic core.

67. (New) A method according to claim 1, wherein said pendant group is independently attached to a ring carbon atom of said A-ring or C-ring, but not of said B-ring.

68. (New) A method according to claim 1, wherein said pendant group is independently attached at one of the "distal" positions of said A-ring or C-ring, which positions are denoted by asterisks (*).

69. (New) A method according to claim 1, wherein said pendant group is independently:
a secondary amino group or
a cationic secondary imino group;
and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is:
a [^{11}C]methyl-labelled tertiary amino group; or
a [^{11}C]methyl-labelled cationic tertiary imino group.

70. (New) A method according to claim 1, wherein said pendant group is independently selected from:

$-\text{NH}_2$, $-\text{NHR}$, $=\text{N}^{(+)}\text{H}_2$, $=\text{N}^{(+)}\text{HR}$, $=\text{NH}$, and $=\text{NR}$;

wherein R is independently selected from C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{1-6} cycloalkyl, and C_{1-6} cycloalkenyl, and is optionally substituted with one or more groups selected from fluoro, chloro, bromo, iodo, hydroxy, and C_{1-4} alkoxy;

and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is:

$-\text{NH}-(^{11}\text{CH}_3)$, $-\text{NR}-(^{11}\text{CH}_3)$, $=\text{N}^{(+)}\text{H}-(^{11}\text{CH}_3)$, $=\text{N}^{(+)}\text{R}-(^{11}\text{CH}_3)$, or $=\text{N}-(^{11}\text{CH}_3)$.

71. (New) A method according to claim 1, wherein said pendant group is independently selected from: $-\text{NHR}$ and $=\text{N}^{(+)}\text{HR}$;

wherein R is independently selected from C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, C_{1-6} cycloalkyl, and C_{1-6} cycloalkenyl, and is optionally substituted with one or more groups selected from fluoro, chloro, bromo, iodo, hydroxy, and C_{1-4} alkoxy;

and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is: $-\text{NR}-(^{11}\text{CH}_3)$ or $=\text{N}^{(+)}\text{R}-(^{11}\text{CH}_3)$.

72. (New) A method according to claim 71, wherein R is independently C_{1-4} alkyl.

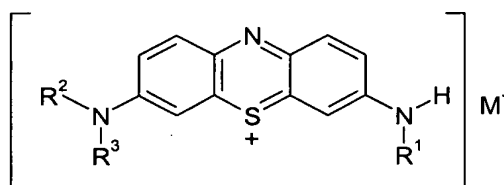
73. (New) A method according to claim 71, wherein R is independently -Me or -Et.

74. (New) A method according to claim 71, wherein R is independently -Me.

75. (New) A method according to claim 1, wherein said compound has, in addition to said pendant group, one or more additional substituents selected from:

amino (-NH₂), methylamino (-NHMe), dimethylamino (-NMe₂), ethylamino (-NH₂Et), diethylamino (-NEt₂), imino (=NH), methylimino (=NMe), ethylimino (=NEt), methyl (-Me), ethyl (-Et), fluoro (-F), chloro (-Cl), bromo (-Br), iodo (-I), oxo (=O), hydroxy (-OH), carboxy (-COOH), and protonated and deprotonated forms thereof.

76. (New) A method according to claim 1, wherein the phenothiazine or phenothiazine-like compound is a compound of the following formula:



wherein:

each of R¹, R², and R³ is independently -H, C₁₋₆alkyl, C₁₋₆alkenyl, C₁₋₆alkynyl, C₁₋₆cycloalkyl, and C₁₋₆cycloalkenyl, and is optionally substituted with one or more groups selected from fluoro, chloro, bromo, iodo, hydroxy, and C₁₋₄alkoxy; and

M⁻ is an anion.

77. (New) A method according to claim 76, wherein -NHR¹ is independently -NHMe.

78. (New) A method according to claim 76, wherein -NR²R³ is independently -NH₂, -NHMe, or -NMe₂.

79. (New) A method according to claim 77, wherein -NR²R³ is independently -NH₂, -NHMe, or -NMe₂.

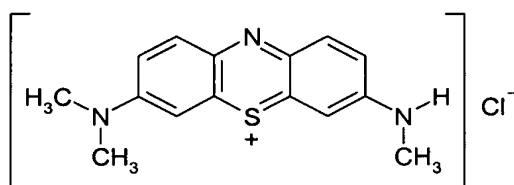
80. (New) A method according to claim 76, wherein -NR²R³ is independently -NMe₂.

81. (New) A method according to claim 77, wherein -NR²R³ is independently -NMe₂.

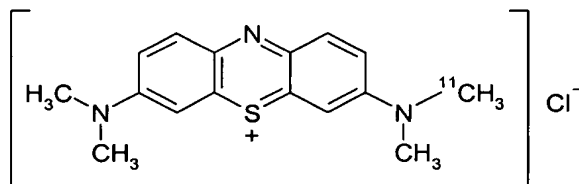
82. (New) A method according to claim 76, wherein M⁻ is independently a halide ion.

83. (New) A method according to claim 77, wherein M⁻ is independently a halide ion.

84. (New) A method according to claim 78, wherein M^- is independently a halide ion.
85. (New) A method according to claim 76, wherein M^- is independently Cl^- .
86. (New) A method according to claim 77, wherein M^- is independently Cl^- .
87. (New) A method according to claim 78, wherein M^- is independently Cl^- .
88. (New) A method according to claim 79, wherein M^- is independently Cl^- .
89. (New) A method according to claim 80, wherein M^- is independently Cl^- .
90. (New) A method according to claim 81, wherein M^- is independently Cl^- .
91. (New) A method according to claim 1, wherein the phenothiazine or phenothiazine-like compound is Azure B:



and said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound is [N-methyl- ^{11}C]methylene blue:



92. (New) A method according to claim 1, wherein said reaction is performed in the presence of a Bronsted base.
93. (New) A method according to claim 1, wherein said reaction is performed in the presence of an alkali metal carbonate or bicarbonate.

94. (New) A method according to claim 1, wherein said reaction is performed in the presence of potassium carbonate.
95. (New) A method according to claim 1, wherein said reaction is carried out in aqueous media.
96. (New) A method according to claim 1, wherein said reaction is carried out by introducing said [¹¹C]methyl trifluoromethanesulfonate into an aqueous solution or suspension of said phenothiazine or phenothiazine-like compound, to form a reaction mixture.
97. (New) A method according to claim 96, wherein said aqueous solution or suspension further comprises a Bronsted base.
98. (New) A method according to claim 96, wherein said aqueous solution or suspension further comprises an alkali metal carbonate or bicarbonate.
99. (New) A method according to claim 96, wherein said aqueous solution or suspension further comprises potassium carbonate.
100. (New) A method according to claim 96, wherein said reaction mixture is mixed for a mixing time of 1-30 minutes.
101. (New) A method according to claim 96, wherein said reaction mixture is mixed for a mixing time of 1-10 minutes.
102. (New) A method according to claim 96, wherein said reaction is carried out at 20°C-25°C.
103. (New) A method according to claim 96, wherein said reaction is carried out under an inert atmosphere.
104. (New) A method according to claim 96, wherein said reaction is carried out under argon.

105. (New) A method according to claim 1, further comprising the subsequent step of:
purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.
106. (New) A method according to claim 1, further comprising the subsequent step of:
purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound
using ion exchange methods.
107. (New) A method according to claim 1, further comprising the subsequent step of:
purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound
using cation exchange methods.
108. (New) A method according to claim 1, wherein the reaction and optional purification
is performed in less than 60 minutes.
109. (New) A method according to claim 1, wherein the reaction and optional purification
is performed in less than 45 minutes.
110. (New) A method according to claim 1, wherein the reaction and optional purification
is performed in less than 40 minutes.
111. (New) A method according to claim 1, which provides a radiochemical purity greater
than 90%.
112. (New) A method according to claim 1, which provides a radiochemical yield of at
least 2%.
113. (New) A method according to claim 1, which provides a specific average activity of
at least 0.5 GBq/ μmol .
114. (New) A method according to claim 1, which is partially or fully automated.
115. (New) A [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound which is
obtained by a method according to claim 1.
116. (New) A composition comprising a compound according to claim 115.

117. (New) A composition comprising a compound according to claim 115 and a pharmaceutically acceptable carrier or excipient.

118. (New) A method of PET imaging which employs a compound according to claim 115.

119. (New) A method of PET imaging comprising the steps of:

- (i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to claim 1;
- (ii) introducing said compound into a subject; and
- (iii) PET imaging the subject.

120. (New) A method of manufacturing a medicament for use in the treatment of skin cancer, melanoma, a tauopathy, or Alzheimer's disease which includes the steps of a method according to claim 1.

121. (New) A method of manufacturing a medicament for use in the diagnosis or prognosis of skin cancer, melanoma, a tauopathy, or Alzheimer's disease which includes the steps of a method according to claim 1.

122. (New) A method of treatment of skin cancer, melanoma, a tauopathy, or Alzheimer's disease in a patient, comprising administering to said patient a therapeutically-effective amount of a compound according to claim 115.

123. (New) A method of treatment of skin cancer, melanoma, a tauopathy, or Alzheimer's disease in a patient, comprising the steps of:

- (i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to claim 1;
- (ii) administering to said patient a therapeutically-effective amount of said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.

124. (New) A method of diagnosis or prognosis of skin cancer, melanoma, a tauopathy, or Alzheimer's disease which employs a compound according to claim 115.

125. (New) A method of diagnosis or prognosis of skin cancer, melanoma, a tauopathy, or Alzheimer's disease comprising the steps of:

(i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to claim 1;

(ii) introducing said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound into the subject;

(iii) determining the presence and/or location and/or amount of [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound in the subject;

(iii) correlating the result of the determination made in (ii) with a disease condition of the subject.